REMARKS

I. Introduction

In response to the Office Action dated March 4, 2009, claim 50 has been cancelled, and claim 26 has been amended. Claims 26-37 and 39-45 remain in the application. Re-examination and re-consideration of the application, as amended, is requested.

II. Claim Amendments

Applicants' attorney has amended claim 26 as indicated above in order to further focus its scope on certain subject matter. The amendment to the chemical formula in claim 26 removes subject matter from this claim and adds no new matter. The amendment relating to treating dyskinesia in a subject, wherein the dyskinesia is manifest as chorea or dystonia is fully supported by the specification as filed and adds no new matter. Support for this subject matter can be found for example in the fourth paragraph on page 7 of the specification.

III. Non-Art Rejections

On pages (4)-(6) of the Office Action, claim 50 was rejected under 35 U.S.C. §112, first paragraph as lacking enablement.

Claim 50 has been cancelled hereinabove. The cancellation of this claim, with traverse, and without acquiescence to the Examiner's rejection, renders this rejection moot.

IV. Prior Art Rejections

On pages (7)-(8) of the Office Action, claims 26, 27, 30, 33-34, 36-37, 39, and 41-45 were rejected under 35 U.S.C. §103(a) as being unpatentable over Chenard et al., EP 0900568 (Chenard) in view of Ling et al., U.S. Patent No. 6,200,970 (Ling).

On pages (8)-(9) of the Office Action, claim 35 was rejected under 35 U.S.C. §103(a) as being unpatentable over Chenard and http://web.archive.org/web/20000815082545/neurologychannel.com/parkinsondisease/index.shtml (PD website).

On pages (9)-(11) of the Office Action, claims 26-34, 36, 37 and 39-45 were rejected under 35 U.S.C. §103(a) as being unpatentable over Leventer, U.S. Patent 6,649,607 (Leventer) and Chenard.

Applicants respectfully traverse these rejections. In the sections below, Applicants' attorney reviews the invention recited in the claims and the references cited by the Patent Office. Applicants' attorney then identifies how these references cannot be used to render the invention recited in the claims obvious.

1. THE CLAIMED INVENTION AND THE CITED REFERENCES

A. The Claimed Invention

The invention recited in claim 26 relates to a method of treating dyskinesia in a subject comprising administering to the subject a therapeutically effective amount of a compound of the formula (I) as defined in claim 26. In this context, those of skill in this art understand that dyskinesias are pathologies that are distinct from other movement disorders such as Parkinson's disease. Those of skill in the art further understand that dyskinesias are a common side-effect of agents (such as L-Dopa) that are used to treat Parkinson's disease.

Claim 26 has been amended hereinabove to focus its scope on dyskinesias that manifest as chorea or dystonia. In addition, claim 26 has been amended hereinabove to focus its scope on a subset of chemical compounds encompassed by the original claims.

B. EP 0900568 to Chenard *et al.*

Chenard *et al.* discloses a method of treating dyskinesias resulting from the use of dopamine agonist therapy by administering AMPA receptor antagonists (see page 2, lines 5 and 6 and page 2, line 47 to page 9, line 53 of Chenard *et al.*). As acknowledged by the Examiner at page 7 of the outstanding Office Action, the AMPA receptor antagonists disclosed in Chenard *et al.* do not correspond to the compounds of the formula (I) as defined in claim 26. There is no teaching or suggestion in Chenard *et al.* that a compound of the formula (I) as defined in claim 26 acts as an AMPA receptor agonist (and/or would be useful in treating dyskinesia).

C. U.S. Patent No. 6,200,970 to Ling et al.

Ling *et al.* discloses 8-alkoxy-substituted 2,3-benzodiazepine derivatives and their use as inhibitors of AMPA receptors and in the treatment of neurological disorders that are triggered by the over stimulation of the AMPA receptor (see column 1, lines 17 to 55 and column 2, line 64 to column 3, line 31 of Ling *et al.*).

There is no disclosure in Ling *et al.* of the use of the derivatives it describes in the treatment of dyskinesia, which is different from the neurodegenerative diseases that are the target of the compounds disclosed in Ling *et al.*

2. APPLICANTS' RESPONSE TO THE REJECTIONS UNDER 35 U.S.C. 103(a)

A. REJECTION TO CLAIMS 26, 27, 30, 33-34, 36-37, 39, and 41-45 IN VIEW OF CHENARD AND LING

In the outstanding rejection under 35 U.S.C. § 103(a), the Patent Office asserts that because Chenard teaches that a dyskinesia can be treated using the AMPA antagonists disclosed therein, it would have been obvious to the skilled person to treat dyskinesias using any one of the various AMPA antagonists that have been described in the art, including those having a completely different chemical formula from the compounds disclosed in Chenard (e.g., those disclosed in Ling).

Applicants traverse this rejection because one of skill in the art would not agree with the technical arguments relied upon by the Patent Office to reject claim 26 under 35 U.S.C. § 103(a). In particular, Applicants respectfully traverse this rejection because it disregards the chemistry and pharmacology of the compounds disclosed in Chenard as compared the chemistry and pharmacology of the compounds that are the subject of the present application (e.g. their respective pharmacological profiles *in vivo*). In this context, those of skill in the art understand that the compounds disclosed for example in Ling only have superficial similarities to the compounds of the formula (I) as defined in claim 26. For example, the skilled artisan will note that the compounds of the formula (I) as defined in claim 26 are a different sub-set of 2,3-benzodiazepines from the AMPA receptor antagonists disclosed in Ling *et al.* and are not AMPA receptor antagonists. In addition, in order to further prosecution of the instant claims, claim 26 has been amended hereinabove so that

the 8-alkoxy-substituted 2,3-benzodiazepine derivatives disclosed in Ling do not correspond to the compounds of formula (I) as recited in amended claim 26. Specifically, Ling teaches that the group X in the 8-alkoxy-substituted 2,3-benzodiazepine derivatives may be hydrogen or halogen. Claim 26 as amended hereinabove excludes these compounds. For the reasons noted above, the skilled person could not have combined the disclosures of Chenard and Ling to arrive at the invention recited in amended claim 26.

In addition, as noted for example in KSR v. Teleflex, 550 U.S. 398, 127 S. Ct. 1727 (2007), in determinations of obviousness under 35 U.S.C. §103(a), there must be some motivation to combine references. As noted by the Examiner, neither Chenard nor Ling teaches or suggests the use of non-AMPA receptor antagonists to treat dyskinesias (much less the specific non-AMPA receptor antagonists that are recited in claim 26). In this context, skilled artisans understand that chemical compounds having different structures correspondingly have different pharmacological properties. For this reason those of skill in this art would not agree with the Patent Office's belief that it is obvious to mix and match the disclosures of Chenard and Ling in a manner that produces the invention recited in claim 26. For example, a physician treating a patient suffering from dyskinesia following a therapeutic regimen that called for a AMPA receptor agonist disclosed in Chenard would not agree that he or she could simply substitute a chemical compound disclosed in Ling because, as the Patent Office asserts, they are "taught to be useful in treating neurodegenerative diseases such as Parkinson's disease" (i.e. at page 8 of the outstanding Office Action). Instead, any physician who believed that would be obvious to treat patients diagnosed with a first neurodegenerative disease (e.g. dyskinesia) with therapeutic agents that are used to treat a completely different type of neurodegenerative diseases (e.g. Parkinson's disease or Alzheimer's disease or Huntington's disease as disclosed in Ling) simply because they are "taught to be useful in treating neurodegenerative diseases such as Parkinson's disease" would have his or her professional competence called into question. For this additional reason, Applicants respectfully request a withdrawal of the rejection to claims 26, 27, 30, 33-34, 36-37, 39, and 41-45 under 35 U.S.C. §103(a).

B. REJECTION TO CLAIM 35 IN VIEW OF CHENARD, LING AND THE PD WEBSITE

For the reasons noted above, Applicants further traverse the rejection to claim 35 as being unpatentable over Chenard in view of Ling as applied to claims 35 in further view of the PD website. As discussed above, the subject matter in claim 35 is non-obvious over the disclosures of Chenard and Ling by virtue of its dependency on claim 26.

In addition, those of skill in this art will note that the "PD Website" is nothing more than a common, superficial dictionary description of Parkinson's disease and cannot remedy the deficiencies in the Chenard and Ling disclosures. For example, it provides no teaching of relevance to the presently claimed invention and certainly provides no teaching or suggestion to use a compound of the formula (I) as defined in amended claim 26 to treat dyskinesia, let alone to specifically treat dyskinesia associated with idiopathic Parkinson's disease. Thus, claim 26 as amended hereinabove and the claims dependent thereon (including claim 35) are non-obvious over the disclosures of Chenard, Ling and the "PD Website".

C. REJECTION TO CLAIMS 26 TO 34, 36, 37 AND 39 TO 45 IN VIEW OF CHENARD AND LEVENTER

Applicants respectfully traverse the rejection based upon a combination of Chenard and Leventer. Leventer teaches the use of S-tofisopam, a benzodiazepine, for treating and preventing convulsions and seizures. Leventer also teaches that S-tofisopam may be administered in combination with one or more other anti-convulsants to treat or prevent convulsions or seizures including myoclonic jerks (see column 1, lines 13 to 40, column 3, lines 11 to 19, column 3, line 51 to column 4, line 16 and column 9, lines 45 to 56 of Leventer). As noted by the Examiner at page 10 of the Office Action, Leventer does not teach the use of S-tofisopam to treat dyskinesia.

Claim 26 as amended now focuses on particular forms of dyskinesia, i.e. chorea and dystonia, disorders of the anatomical region of the brain termed the basal ganglia. The underlying mechanisms by which chorea and dystonia are produced are known and are different from the mechanisms underlying epileptic or convulsive activity (i.e. the focus of Leventer). This fundamental difference is shown for example when one compares the therapeutic agents used to treat myoclonus with those used to treat chorea and/or dystonia. In particular, myoclonus is treated with tranquilizers and anticonvulsants. Chorea and dystonia are not. Chorea can be abolished with dopamine receptor antagonists but there is no really effective medical treatment for dystonia. Thus,

the Examiner's reliance on the pathologically broad definitions included in the Chenard patent is misplaced and those of skill in this art would not therefore agree with the Patent Office's belief that it is obvious to mix and match the disclosures of Chenard and Leventer in a manner that produces the invention recited in claim 26

In the outstanding rejection the Examiner considers that it would have been obvious to use S-tofisopam to treat dyskinesia because S-tofisopam is known from Leventer to treat convulsions and seizures and further because Chenard teaches that dyskinesia is defined as any abnormal or uncontrollable movement including chorea, tremor, dystonia, athetosis, myoclonus and tic. Applicants respectfully traverse this rejection because one of skill in the art would not agree with the technical accuracy of the Chenard patent. In particular, while the drafter of the Chenard patent followed a not uncommon patent practice of broadly defining terms (e.g. defining the term "dyskinesia" to encompass all forms of abnormal movement including for example myoclonus), those of skill in the art would immediately point out that there is no scientific justification for this definition. In fact, this definition is contrary to accepted teachings in this technology. For example, artisans in this field make a clear distinction between myoclonus and dyskinesia (conditions which are linked in the Chenard patent). Specifically, dyskinesias are clinically defined as: "abnormal, involuntary body movements that can appear as jerking, fidgeting, twisting, and turning movements". In contrast myoclonic jerks are a separate clinical phenomena, one characterized by sudden contractions of the big body muscles. Myoclonic jerks typically occur when a subject is falling asleep and cause a feeling of stumbling, falling or similar that subsequently cause a subject to wake up again. While almost everyone has experienced a myoclonic jerk while falling asleep, a professionally competent physician informed of this experience would not diagnose and then begin to treat dyskinesia in such individuals.

As noted above, those of skill in the art understand that there is a clear distinction between: (1) myoclonus (myoclonic jerks), convulsive activity, epileptic activity and seizures; and (2) dyskinesia manifest as chorea or dystonia. This distinction is confirmed by Lavender's disclosure that that informs artisans that the convulsions and seizures it describes are commonly associated with epilepsy (see column 8, line 31 to column 9, line 10 of Leventer). For this reason, neither Leventer nor Chenard teaches or suggests the use of S-tofisopam, or any other compound of the formula (I) as defined in amended claim 26, to treat dyskinesia. In this context, as noted for

example in MPEP §2142 and 2143.03, to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art (see, e.g. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)). As noted above, however, the invention recited in claim 26 as amended hereinabove cannot be generated by a combination of the Leventer and Chenard disclosures. For this additional reason, Applicants respectfully request a withdrawal of the rejection to claim 26 under 35 U.S.C. §103(a). Claims 27 to 37 and 39 to 45 also are non-obvious over the disclosures of these documents by virtue of their (direct or indirect) dependency on amended claim 26.

D. REJECTION IN VIEW OF CHENARD AND LEVENTER. AND THE "PD WEBSITE"

For the reasons noted above, Applicants further traverse the rejection to claim 35 as being unpatentable over Chenard in view of Leventer as applied to claims 35 in further view of the PD website. As discussed above, the subject matter in claim 35 is non-obvious over the disclosures of Chenard and Leventer by virtue of its dependency on claim 26.

In this rejection, the Examiner asserts that the "PD Website" teaches that the most common type of Parkinson's disease is idiopathic Parkinson's disease and seems to suggest that when treating dyskinesia associated with parkinsonism, then the parkinsonism would necessarily be idiopathic Parkinson's disease. However, as discussed above, the "PD Website" is nothing more than a common, superficial dictionary description of Parkinson's disease and cannot remedy the deficiencies in the Chenard and Leventer disclosures. For example, it provides no teaching of relevance to the presently claimed invention and certainly provides no teaching or suggestion to use a compound of the formula (I) as defined in amended claim 26 to treat dyskinesia, let alone to specifically treat dyskinesia associated with idiopathic Parkinson's disease. Thus, amended claim 26 and the claims dependent thereon (including claim 35) are non-obvious over the disclosures of Leventer and Chenard and the "PD Website".

In summary, independent claim 26 is allowable over Chenard and Ling, either alone, or in combination with other disclosures such as those found in "PD website" and/or Leventer. Further, the dependent claims are submitted to be allowable over these disclosures in the same manner, because they are dependent on independent claim 26 and thus contain all the limitations of these

independent claims. In addition, the dependent claims further recite constellations of novel elements not shown by Chenard, Ling, Leventer and/or the "PD website". Moreover, the various elements of Applicants' claimed invention together provide operational advantages over Chenard, Ling, PD website and Leventer. In addition, Applicants' invention solves problems not recognized by Chenard, Ling, PD website and Leventer.

V. Conclusion

In view of the above, it is submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,

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